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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/057,409	01/23/2002	Maria Palasis	BSX:236US2	1618

32425 7590 09/06/2007
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EXAMINER	
KELLY, ROBERT M	
ART UNIT	**PAPER NUMBER**
1633	

MAIL DATE	DELIVERY MODE
09/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/057,409	PALASIS, MARIA	
	Examiner	Art Unit	
	Robert M. Kelly	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-11,15-22,24,26-38,40-48 and 52-62* is/are pending in the application.

4a) Of the above claim(s) *4-11,16,18,20-22,26-37,41-48,52 and 53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15,17,19,24,38,40 and 54-62* is/are rejected.

7)☒ Claim(s) *4-11,16,18,20-22,26-37,41-48 and 52-54* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and argument of 6/28/07 are entered.

Claims 15, 17, 19, and 38 are amended.

Claim 25 is cancelled.

Claims 55-62 are newly presented

Claims 4-11, 15-22, 24, 26-38, 40-48, and 52-62 are presently pending.

Election/Restrictions

In keeping with the prior restriction requirement, Claims 15, 17, 19, 24, 38, 40, and 54-62 are presently considered, with respect to the elected invention, and the balance of the presently pending are withdrawn as being drawn to non-elected inventions.

Claim Status, Cancelled Claims

In light of Applicant's cancellation of Claims 25, all rejections and/or objections to such claims are withdrawn.

Claim Objections

Claim 54 is objected to for depending from a non-elected invention (Claim 21), and is only considered with regard to the limitations of the elected invention.

Claims 4-11, 16, 18, 20-22, 26-37, 41-48, and 52-54 are objected as being drawn to or encompassing non-elected inventions.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In light of the amendments, the rejections of record for Claims 15, 17, 19, 23-24, 38, 40, 50-51, and 54 under 35 U.S.C. 112, first paragraph, because the specification, as not having enablement for the absence of a transgene, are withdrawn; however:

Claims 17 and 24 remain, and Claims 57-58 are newly, rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods wherein the transgene is expressed by the BMS cells, does not reasonably provide enablement for the absence of expression, for reasons of record. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

It is noted that Claim 17, from which the other claims depend, does not require the transgene to be expressed, and when considered in the context of the other independent claims, e.g., Claims 15, 19, and 38, which each require the transgene to be expressed, indicates that Claim 17, and its dependent claims, do not require such expression, and is specifically being claimed.

Hence, for reasons of record, these claims are rejected as lacking enablement for an absence of expression of the angiogenic factor, as such cases would require undue experimentation to find those embodiments which would still be efficacious in the therapy.

Response to Argument – Enablement

Applicant's argument of 6/28/07 has been fully considered but is not found persuasive.

Applicant argues other issues, and does not argue that the absence of expression is possible in the therapeutic methods, and hence, the Argument is non-persuasive.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

In light of the amendments, the rejections of Claims 15, 17, 19, 24, 25, 38, 40 and 54 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 7,097,832 to Kornowski, et al., Patented 8/29/06, and claiming priority to at least 8/5/00, are withdrawn.

Specifically, Applicant has excluded HIF from the claims, and further requires a transgene to express the angiogenic protein from a list not containing HIF. Therefore, the claims can no longer be rejected as anticipated by Kornowski.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim15, 17, 19, 24, 25, 38, 40, 54, 55, 57, 59, and 61 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 7,097,832 to Kornowski, et al., Patented 8/29/06, and claiming priority to at least 8/5/00 and U.S. Patent No. 7,186,688 and U.S. Patent No. 7,186,688 to Hu, et al.

With regard to Claims 15, 17, 19, 38, 55, 57, 59, and 61, Kornowski teaches treatment of myocardial conditions with administration of autologous bone marrow (e.g., ABSTRACT), which may carry a transgene for an angiogenic growth factor, including HIF-1 (e.g., ABSTRACT; col. 2, paragraph 6). The bone marrow cells which may be transformed include the stromal cells (e.g., col. 16, paragraph 2). Further, the cells may be administered to tissue adjacent ischemic tissue (e.g., col. 15, paragraph 4). Such may be done to increase collateral blood vessel formation (e.g., col. 1, paragraph 2) and induce angiogenesis (e.g., col. 2, paragraph 3), and increase contractile function (e.g., EXAMPLE 4), in an ischemic heart myocardium (e.g., col. 2, paragraph 6). Moreover, the cells are modified to comprise the transgene *ex vivo* with e.g., a plasmid or adenoviral vector comprising the angiogenic transgene (e.g., col. 16, paragraph 2). Also, such HIF-1 production increases VEGF levels produced by the cells (e.g., col. 16, paragraph 2 and Claim 8), thereby modifying the cells to produce multiple angiogenic factors, including HIF-1 and VEGF. Still further, Kornowski teaches treatment of humans (EXAMPLE 6), with autologous cells (e.g., TITLE). Lastly, Kornowski teaches that such strategies can be simply to increase the production of VEGF and/or other cytokines with angiogenic activity (col. 16, paragraph 2).

With regard to Claims 24 and 40, the cells may be injected into multiple sites, including multiple sites adjacent to the ischemic zone (e.g., EXAMPLE 4).

With regard to Claim 54, the injection may be made by catheter (e.g., col. 10, paragraph 2).

However, Kornowski does not specifically teach the use of a VEGF transgene, but only recognizes that such is successful to treat ischemic heart when administered transgenically via adenoviral vectors (e.g., cols. 1-2, paragraph bridging).

On the other hand, Hu teaches VEGF transgenes which can be used for angiogenic therapy in the myocardium (e.g., CLAIMS and col. 38, paragraph 5 and cols. 40-42).

Hence, at the time of invention, it would have been obvious to modify the methods of Kornowski with the VEGF transgene of Hu. The Artisan would have been motivated to do so as it was already known in the Art that VEGF transgenes could also produce beneficial effects to treat ischemic heart and Kornowski taught that other methods of increasing this factor's production would be successful and Hu demonstrates that the production of such protein can treat myocardium. Moreover, the Artisan would have had a reasonable expectation of success, as it was known in the art that VEGF was sufficient to produce increased angiogenesis.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 15, 17, 19, 24, 25, 38, 40, 54, 55, 57, 59, and 61 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 7,097,832 to Kornowski, et al., Patented 8/29/06, and claiming priority to at least 8/5/00, and Safi, et al. (1999) Microvascular Resesearch, 58: 238-49.

With regard to Claims 15, 17, 19, 38, 55, 57, 59, and 61, Kornowski teaches treatment of myocardial conditions with administration of autologous bone marrow (e.g., ABSTRACT), which may carry a transgene for an angiogenic growth factor, including HIF-1 (e.g., ABSTRACT; col. 2, paragraph 6). The bone marrow cells which may be transformed include the stromal cells (e.g., col. 16, paragraph 2). Further, the cells may be administered to tissue adjacent ischemic tissue (e.g., col. 15, paragraph 4). Such may be done to increase collateral blood vessel formation (e.g., col. 1, paragraph 2) and induce angiogenesis (e.g., col. 2, paragraph 3), and increase contractile function (e.g., EXAMPLE 4), in an ischemic heart myocardium (e.g., col. 2, paragraph 6). Moreover, the cells are modified to comprise the transgene *ex vivo* with e.g., a plasmid or adenoviral vector comprising the angiogenic transgene (e.g., col. 16, paragraph 2). Also, such HIF-1 production increases VEGF levels produced by the cells (e.g., col. 16, paragraph 2 and Claim 8), thereby modifying the cells to produce multiple angiogenic factors, including HIF-1 and VEGF. Still further, Kornowski teaches treatment of humans (EXAMPLE 6), with autologous cells (e.g., TITLE). Lastly, Kornowski teaches that such strategies can be simply to increase the production of VEGF and/or other cytokines with angiogenic activity (col. 16, paragraph 2).

With regard to Claims 24 and 40, the cells may be injected into multiple sites, including multiple sites adjacent to the ischemic zone (e.g., EXAMPLE 4).

With regard to Claim 54, the injection may be made by catheter (e.g., col. 10, paragraph 2).

However, Kornowski does not specifically teach the use of a FGF-1 transgene, but only recognizes that such is successful to treat ischemic heart when administered transgenically via adenoviral vectors (e.g., col. 1, paragraph 3).

Moreover, at the time of invention, it had been shown in even more models that FGF, expressed transgenically in live tissue adjacent ischemic heart could increase angiogenesis and improve various parameters demonstrating improvements (e.g., Safi, et al. (1999) Microvascular Research, 58: 238-49, article in general, discussion in particular).

Hence, at the time of invention, it would have been obvious to modify the methods of Kornowski with the FGF-1 transgenes of Safi. The Artisan would have been motivated to do so as it was already known in the Art that FGF-1 transgenes could also produce beneficial effects to treat ischemic heart. Moreover, the Artisan would have had a reasonable expectation of success, as many models had demonstrated increased angiogenesis.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 15, 17, 19, 38, 24, 54, 56, 58, 60, and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 7,097,832 to Kornowski, et al., Patented 8/29/06 and U.S. Patent No. 7,186,688 to Hu, et al., as applied to claims 15, 17, 19, 24, 25, 38, 40, 54, 55, 57, 59, and 61 above, and further in view of U.S. Patent No. 5,800,539 to Waller; and

Claims 15, 17, 19, 38, 24, 54, 56, 58, 60, and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 7,097,832 to Kornowski, et al., Patented 8/29/06, and claiming priority to at least 8/5/00, and Safi, et al. (1999) Microvascular Resesearch, 58: 238-49, as applied to claims 15, 17, 19, 24, 25, 38, 40, 54, 55, 57, 59, and 61 above, and further in view of U.S. Patent No. 5,800,539 to Waller.

As shown above, Kornowski and Hu or Kornowski and Saffi each make obvious the various aspects of the invention, except that of the use of allogenic BMS cells.

However, Waller teaches the use of allogenic BMS cells for transplantation (e.g., ABSTRACT; CLAIMS). Moreover, such can be performed without lethal graft versus host disease (ABSTRACT).

Hence, at the time of invention it would have been obvious to modify Kornowski or Kornowski/Saffi with the allogenic BMS of Waller. The Artisan would have been motivated to do so because Waller teaches that such may be performed with causing lethal graft versus host disease. Moreover, the Artisan would have had a reasonable expectation of success, as Kornowski and Kornowski/Saffi had demonstrated that the transplant would be efficacious and Waller teaches that allogenic cells could be used in transplants.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert M. Kelly, Art Unit 1633, whose telephone number is (571) 272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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